





DATE: 06/21/2002

TIME: 14:06:57

PATENT APPLICATION: US/09/668,314B

RAW SEQUENCE LISTING

Input Set : A:\6280NCP.txt Output Set: N:\CRF3\06212002\1668314B.raw 5 <110> APPLICANT: Gurney, et al 8 <120> TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES THEREOF 12 <130> FILE REFERENCE: 28341/6280NCP 15 <140> CURRENT APPLICATION NUMBER: US 09/668,314B 7 > 16 <141 > CURRENT FILING DATE: 2002-06-11 19 <150> PRIOR APPLICATION NUMBER: US 60/169,232 20 <151> PRIOR FILING DATE: 1999-12-06 23 <150> PRIOR APPLICATION NUMBER: US 09/416,901 24 <151> PRIOR FILING DATE: 1999-10-13 27 <150> PRIOR APPLICATION NUMBER: US 60/155,493 28 <151> PRIOR FILING DATE: 1999-09-23 31 <150> PRIOR APPLICATION NUMBER: US 09/404,133 32 <151> PRIOR FILING DATE: 1999-09-23 35 <150> PRIOR APPLICATION NUMBER: PCT/US99/20881 36 <151> PRIOR FILING DATE: 1999-09-23 39 <150> PRIOR APPLICATION NUMBER: US 60/101,594 40 <151> PRIOR FILING DATE: 1998-09-24 43 <160> NUMBER OF SEQ ID NOS: 83 46 <170> SOFTWARE: PatentIn version 3.1 49 <210> SEO ID NO: 1 50 <211> LENGTH: 1804 51 <212> TYPE: DNA 52 <213> ORGANISM: Homo sapiens 54 <400> SEQUENCE: 1 55 atgggcgcac tggcccgggc gctgctgctg cctctgctgg cccagtggct cctgcgcgcc 60 57 geoceggage tggcccccgc geocttcacg etgcccctcc gggtggccgc ggccacgaac 120 59 egegtagttg egeceaece gggaeceggg acceetgeeg agegeeaege egaeggettg 180 61 gegetegeee tggageetge eetggegtee eeegegggeg eegeeaactt ettggeeatg 240 63 gtagacaacc tgcaggggga ctctggccgc ggctactacc tggagatgct gatcgggacc 300 65 cccccgcaga agctacagat tctcgttgac actggaagca gtaactttgc cgtggcagga 360 67 accccgcact cctacataga cacgtacttt gacacagaga ggtctagcac ataccgctcc 420 69 aagggetttg acgteacagt gaagtacaca caaggaaget ggaegggett egttggggaa 480 71 gacctegtea ccatececaa aggetteaat aettetttte ttgteaacat tgeeactatt 540 73 tttgaatcag agaatttctt tttgcctggg attaaatgga atggaatact tggcctagct 600

75 tatgccacac ttgccaagcc atcaagttct ctggagacct tcttcgactc cctggtgaca

77 caagcaaaca teeccaacgt tttetecatg cagatgtgtg gageeggett geeegttget

79 qqatctqqqa ccaacqqaqq taqtcttqtc ttqqqtqqaa ttqaaccaaq tttqtataaa

81 ggagacatct ggtatacccc tattaaggaa gagtggtact accagataga aattctgaaa

83 ttggaaattg gaggccaaag cettaatetg gactgcagag agtataacgc agacaaggcc

85 atcgtggaca gtggcaccac gctgctgcgc ctgccccaga aggtgtttga tgcggtggtg

87 gaagetgtgg cccgcgcatc tetgatteca gaattetetg atggtttetg gaetgggtee

89 cagctggcgt gctggacgaa ttcggaaaca ccttggtctt acttccctaa aatctccatc

660

720

780

840

900

960

1020

1080

Input Set : A:\6280NCP.txt

Output Set: N:\CRF3\06212002\1668314B.raw

93 95 97 99 101 103 105 107 111 113 115 118	atto teca agage gtgt cag gec age get ctc aaa <21	agececececececececececececececececececec	ca to the transfer of the tran	gatg gatg gagg ttcc gcga ttgt acct acct	gggggggggggggggggggggggggggggggggggggg	c cgo t cgo g ct c tt at co aa to ca ao tg go ga t	geet gtge tete tete gtee gatg ceat eget	gaat cacg agcg aaca ggatt tgctg agtco tgtct tgtct	tate gtg agce gage t gte g cte t cae t cte t tte	gaate atgga cccte gatge gctge tctge gcta gtgat	gtt a agg of tag of tatg ccgt gtca ttaa ccac	accga gette caga ccage cget gaca gaaa ccgf	atto ctace aatte caace ggtg atcge aatce tctte	gg cogt cogt cogt cogt cogt cogt cogt co	attto atcto ggtgo gtcco gcgto gcgto tctco cttto	tttac ccca tcgac ctgca ccgct tgtgga cgccc tgaata cagggc tgttct caaatc aaaaa	1140 1200 1260 1320 1380 1440 1500 1560 1620 1680 1740 1800
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121 <213> ORGANISM: Homo sapiens 123 <400> SEQUENCE: 2																	
						3		<b>.</b>	<b>r</b>	<b>.</b>	<b>5</b>	<b>.</b>	<b>.</b>			m	
	Met	GIA	Ата	ьeu	_	Arg	Ата	ьeu	Leu		Pro	ьeu	ьeu	Ата		Trp	
126		т о	7	3 1 a	5	Dwa	<b>a</b> 1	T	3 1 a	10	77.	D	Dh.	m 1	15	Desc	
130	Leu	ьeu	Arg		Ата	PIO	GIU	ьeu	25	PLO	Ald	Pro	Pne	30	Leu	Pro	
	Leu	7 ~~	บาไ	20	λla	ת 1 ת	Πh.~	Nan		W-1	37 - 1	7 l n	Dro		Dwo	C1**	
134	Leu	Arg	35	Ата	Ald	Ата	TIII	40	Arg	vaı	Val	Ата	45	THE	PIO	GIY	
	Dro	C1.		Dwo	21-	C1	A mar		ה I ה	N an	C1	T ou		Ton	71-	Tou	
138	Pro	50	1111	PIO	нта	GIU	55	птъ	Ата	ASP	СТУ	60	Ата	Leu	Ата	Leu	
	Glu		λla	Lou	λla	Sor		λla	C117	λla	λla		Dho	Tou	λla	Mot	
142		FIO	Ата	Deu	Аца	70	PIO	Ада	СТУ	Ата	75	ASII	FIIC	цец	Ата	80	
	Val	Δen	Δcn	T.011	Gln		Δen	Ser	Glv	Δra		Тυν	Ͳτ៸·ϒ	Τ.Δ11	Glu		
146	,	шор	11011	LCu	85		1101	DCI	017	90	O <sub>T</sub>	- 1 -	- 1 -	пси	95	nec	
	Leu	Ile	Glv	Thr		Pro	Gln	Lvs	Leu		Ile	Leu	Va l	Asp		Glv	
150			1	100				-1-	105	~				110		J-1	
	Ser	Ser	Asn		Ala	Val	Ala	Glv		Pro	His	Ser	Tvr		Asp	Thr	
154			115					120					125	-			
	Tyr	Phe	Asp	Thr	Glu	Arg	Ser		Thr	Tyr	Arq	Ser	Lys	Gly	Phe	Asp	
158	-	130	-			_	135			-	_	140	•	•		•	
161	Val	Thr	Val	Lys	Tyr	Thr	Gln	Gly	Ser	Trp	Thr	Gly	Phe	Val	Gly	Glu	
	145				_	150		_		-	155	-			-	160	
165	Asp	Leu	Val	Thr	Ile	Pro	Lys	Gly	Phe	Asn	Thr	Ser	Phe	Leu	Val	Asn	
166	_				165		_	_		170					175		
169	Ile	Ala	Thr	Ile	Phe	Glu	Ser	Glu	Asn	Phe	Phe	Leu	Pro	Gly	Ile	Lys	
170				180					185					190			
173	Trp	Asn	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Thr	Leu	Ala	Lys	Pro	Ser	
174			195					200					205				
177	Ser	Ser	Leu	$\operatorname{Glu}$	Thr	Phe	Phe	Asp	Ser	Leu	Val	Thr	Gln	Ala	Asn	Ile	
178		210					215					220					
	Pro		Val	Phe	Ser		Gln	Met	Cys	Gly	Ala	Gly	Leu	Pro	Val	Ala	
182	225					230					235					240	
	Gly																

Input Set : A:\6280NCP.txt

Output Set: N:\CRF3\06212002\I668314B.raw

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189 Ser Leu Tyr Lys Gly Asp Ile Trp Tyr Thr Pro Ile Lys Glu Glu Trp
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193 Tyr Tyr Gln Ile Glu Ile Leu Lys Leu Glu Ile Gly Gly Gln Ser Leu
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                                                  285
           275
197 Asn Leu Asp Cys Arg Glu Tyr Asn Ala Asp Lys Ala Ile Val Asp Ser
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201 Gly Thr Thr Leu Leu Arg Leu Pro Gln Lys Val Phe Asp Ala Val Val
                                           315
                       310
205 Glu Ala Val Ala Arg Ala Ser Leu Ile Pro Glu Phe Ser Asp Gly Phe
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                                       330
206
209 Trp Thr Gly Ser Gln Leu Ala Cys Trp Thr Asn Ser Glu Thr Pro Trp
                                   345
210
               340
213 Ser Tyr Phe Pro Lys Ile Ser Ile Tyr Leu Arg Asp Glu Asn Ser Ser
                                                   365
           355
                               360
217 Arg Ser Phe Arg Ile Thr Ile Leu Pro Gln Leu Tyr Ile Gln Pro Met
       370
                           375
221 Met Gly Ala Gly Leu Asn Tyr Glu Cys Tyr Arg Phe Gly Ile Ser Pro
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                                           395
225 Ser Thr Asn Ala Leu Val Ile Gly Ala Thr Val Met Glu Gly Phe Tyr
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                                       410
229 Val Ile Phe Asp Arg Ala Gln Lys Arg Val Gly Phe Ala Ala Ser Pro
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233 Cys Ala Glu Ile Ala Gly Ala Ala Val Ser Glu Ile Ser Gly Pro Phe
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234
           435
237 Ser Thr Glu Asp Val Ala Ser Asn Cys Val Pro Ala Gln Ser Leu Ser
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241 Glu Pro Ile Leu Trp Ile Val Ser Tyr Ala Leu Met Ser Val Cys Gly
                       470
                                           475
245 Ala Ile Leu Leu Val Leu Ile Val Leu Leu Leu Pro Phe Arg Cys
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                                       490
249 Gln Arg Arg Pro Arg Asp Pro Glu Val Val Asn Asp Glu Ser Ser Leu
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               500
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254
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259 <212> TYPE: DNA
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265 ggcacccagc acggcatccg gctgcccctg cgcagcggcc tggggggcgc cccctgggg
                                                                       120
180
269 gtggagatgg tggacaacct gaggggcaag tcggggcagg gctactacgt ggagatgacc
                                                                       240
                                                                       300
271 gtgggcagcc ccccgcagac gctcaacatc ctggtggata caggcagcag taactttgca
273 gtgggtgctg cccccaccc cttcctgcat cgctactacc agaggcagct gtccagcaca
                                                                       360
275 taccgggacc tccggaaggg tgtgtatgtg ccctacaccc agggcaagtg ggaaggggag
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277 ctqqqcaccq acctqqtaaq catcccccat ggccccaacg tcactqtqcq tgccaacatt
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279 gctqccatca ctgaatcaga caagttette atcaaegget ccaaetggga aggeateetg
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Input Set : A:\6280NCP.txt

Output Set: N:\CRF3\06212002\1668314B.raw

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                                                                         660
285 cccctcaacc agtctgaagt gctggcctct gtcggaggga gcatgatcat tggaggtatc
                                                                         720
287 gaccactege tgtacacagg cagtetetgg tatacaceca teeggeggga gtggtattat
                                                                         780
289 gaggtcatca ttgtgcgggt ggagatcaat ggacaggatc tgaaaatgga ctgcaaggag
                                                                         840
291 tacaactatg acaagagcat tgtggacagt ggcaccacca accttcgttt gcccaagaaa
                                                                         900
293 gtgtttgaag ctgcagtcaa atccatcaag gcagcctcct ccacggagaa gttccctgat
                                                                        960
295 ggtttctggc taggagagca gctggtgtgc tggcaagcag gcaccacccc ttggaacatt
                                                                        1020
297 ttcccagtca tctcactcta cctaatgggt gaggttacca accagtcctt ccgcatcacc
                                                                        1080
299 atccttccgc agcaatacct gcggccagtg gaagatgtgg ccacgtccca agacgactgt
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301 tacaagtttg ccatctcaca gtcatccacg ggcactgtta tgggagctgt tatcatggag
                                                                        1200
303 ggcttctacg ttgtctttga tcgggcccga aaacgaattg gctttgctgt cagcgcttgc
                                                                        1260
305 catgtgcacg atgagttcag gacggcagcg gtggaaggcc cttttgtcac cttggacatg
                                                                       1320
307 gaagactgtg gctacaacat tccacagaca gatgagtcaa ccctcatgac catagcctat
                                                                       1380
309 gtcatggctg ccatctgcgc cctcttcatg ctgccactct gcctcatggt gtgtcagtgg
                                                                       1440
311 cgctgcctcc gctgcctgcg ccagcagcat gatgactttg ctgatgacat ctccctgctg
                                                                       1500
313 aagtgaggag geeeatggge agaagataga gatteeeetg gaccacacet eegtggttea
                                                                       1560
315 ctttggtcac aagtaggaga cacagatggc acctgtggcc agagcacctc aggaccctcc
                                                                       1620
317 ccacccacca aatgcctctg ccttgatgga gaaggaaaag gctggcaagg tgggttccag
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319 ggactgtacc tgtaggaaac agaaaagaga agaaagaagc actctgctqq cqqqaatact
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321 cttggtcacc tcaaatttaa gtcgggaaat tctgctgctt gaaacttcag ccctgaacct
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1860
325 gtactggcat cacacgcagg ttaccttggc gtgtgtccct gtggtaccct ggcagagaag
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327 agaccaaget tgttteeetg etggeeaaag teagtaggag aggatgeaca gtttgetatt
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329 tgctttagag acagggactg tataaacaag cctaacattg gtgcaaagat tgcctcttga
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337 <213> ORGANISM: Homo sapiens
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345 Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
346
                20
                                    25
349 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
350
            35
                                40
353 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
354
                            55
357 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
                        70
                                           75
361 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
362
                    85
                                       90
365 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
                100
                                   105
369 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
370
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                               120
373 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
374
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Input Set : A:\6280NCP.txt

Output Set: N:\CRF3\06212002\1668314B.raw

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377 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
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381 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
                   165
                                       170
385 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg'Pro Asp Asp
           180
                                  185
389 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
    195
                               200
393 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
                           215
397 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
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398 225
401 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
                   245
                                       250
405 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
               260
                                   265
409 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
          275
                              280
413 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
                           295
417 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
418 305
                       310
                                           315
421 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
                   325
                                       330
425 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
               340
                                   345
                                                      350
429 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
                               360
433 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
                           375
                                               380
437 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
                       390
                                           395
441 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
                   405
                                       410
445 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
               420
                                   425
449 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
     435
                               440
                                   •
453 Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
                           455
457 Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
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461 Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp
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469 <210> SEQ ID NO: 5
470 <211> LENGTH: 1977
471 <212> TYPE: DNA
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RAW SEQUENCE LISTING ERROR SUMMARY
PATENT APPLICATION: US/09/668,314B

DATE: 06/21/2002
TIME: 14:06:58

Input Set : A:\6280NCP.txt

Output Set: N:\CRF3\06212002\1668314B.raw

## Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the  $\langle 220 \rangle$  to  $\langle 223 \rangle$  fields of each sequence which presents at least one n or Xaa.

Seq#:83; Xaa Pos. 1,2,3,4

VERIFICATION SUMMARY

DATE: 06/21/2002

PATENT APPLICATION: US/09/668,314B

TIME: 14:06:58

Input Set : A:\6280NCP.txt

Output Set: N:\CRF3\06212002\1668314B.raw

L:16 M:271 C: Current Filing Date differs, Replaced Current Filing Date L:5842 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:83 after pos.:0